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Successful Treatment of Orbital Rhabdomyosarcoma in Two Infants Using Chemotherapy Alone

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Two infants, 2 months and 13 months of age, were found to have orbital embryonal rhabdomyosarcomas (ERMS). Because of the adversities associated with either surgical exenteration or curative doses of radiation therapy, they were treated with chemotherapy alone. They survive disease-free 5 and 9 years after diagnosis with excellent cosmesis and normal vision. This approach may be suitable for similarly small (<2 cm in diameter) ERMS in other sites.

Key words: childhood cancer, needle biopsy, facial bone development, soft-tissue sarcoma

INTRODUCTION

Major advances have been made in the management of children with embryonal rhabdomyosarcoma (ERMS) since the advent of effective chemotherapy [1,2]. Radical surgical removal has been replaced by more conservative operations, designed to conserve organs and their function [3,4]. High doses of radiation therapy (RT) to large volumes have been reduced to more moderate levels [5,6]. These improvements have benefited children, especially infants, with orbital ERMS, who no longer suffer the mutilations occasioned by exenteration of the orbital contents and/or high dose RT to the region. Still, growth disturbances and cataracts can occur in children, even after moderate dose RT [7,8]. There is also the persisting danger of radiation-associated second malignant neoplasms, known to occur particularly after RT to the head and neck region even at low doses [9–11].

To avoid these unfortunate sequelae, attempts have been made to use chemotherapy alone in managing ERMS in various parts of the body, including the orbit, with mixed results [12–14]. In most instances, these tumors are larger than those encountered in the orbits of infants, however. We therefore considered it justifiable to try only chemotherapy in two infants with orbital ERMS, the first of these 9 years ago, with the informed consent of the parents.

DESCRIPTION OF PATIENTS

Case 1: LGB

A 2-month-old girl presented with a hemorrhagic nodule at the level of the lower right eyelid that was diagnosed as a hemangioma. In a short period, the tumor increased greatly in size and she was admitted to our hospital in April 1986. Physical examination revealed no abnormalities except for the right orbit (Fig. 1). There was extensive edema of the lids and orbital contents. A hard tumor was present in the lower right eyelid extending to the inner part of the orbit where it could not be felt. The globe was displaced upward with limitation of downward motion.

X-ray examination showed blurring of the lower border of the right orbit that presented a circumference very much bigger than that of the left. A CT scan revealed an extra-ocular expansile process that destroyed the orbital margin of the right maxillary sinus and the posterior portions of the bony orbit. It produced severe exophthalmos and displacement of the globe downwards and outwards. No cleavage plane could be determined between the eye and the tumor. A biopsy was performed and revealed ERMS (Fig. 2).

Treatment was initiated using multiple agent chemotherapy. Two cycles of T-6 were followed by four of T-6M, following the T-6 and T-6M regimens described by Memorial Sloan-Kettering Cancer Center investigators [15].

There was remarkable improvement soon after the start of chemotherapy, with reduction of edema and tu-

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Fig. 1. Case 1. Exophthalmos, with edema and suffusion of the lids and conjunctiva, right eye.

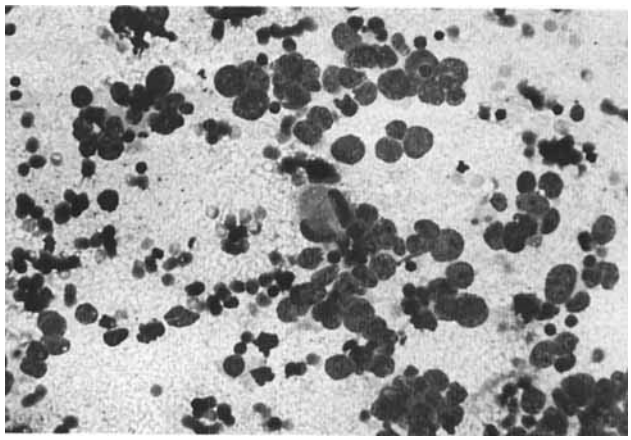

Fig. 2. Case 1. Cytology (needle aspirate). Embryonal rhabdomyosarcoma. Multiple moderate-sized undifferentiated cells with darkly staining nuclei. One large cell with bilobed nucleus is visible in the center of the field.

mor size, and return of normal function. The bony defect remineralized, and no abnormalities were apparent on ophthalmologic examination a year after diagnosis. CT scan at the same time showed an 8mm tumor posterior and inferior to the globe. Biopsy showed only fibrosis without evidence of neoplastic cells.

The patient has remained asymptomatic 9 years from diagnosis.

Case 2: ACM

A 13-month-old boy presented with a 15-day history of left-sided exophthalmos. Physical examination was normal except for eyelid edema, displacement of the eye downwards and outwards, and partial restriction of extraocular movement (Fig. 3). Ultrasonography showed an

Fig. 3. Case 2. Lateral and inferior displacement of the left eye with lid edema and exophthalmos.

orbital mass affecting the internal, and partially the superior, rectus muscles. CT scan showed an extraocular mass that was well-encapsulated and occupied the whole medial wall of the left orbit. No bone erosion was seen.

Biopsy revealed ERMS (Fig. 4) and aggressive multiagent chemotherapy was initiated as in Case 1; i.e., two cycles of T-6 followed by four of T-6M. There again was prompt and remarkable improvement. Clinical, ophthalmologic, echographic, and CT examinations were normal 4 months after the start of treatment.

The patient is currently alive with only strabismus and no evidence of disease 5 years after diagnosis.

DISCUSSION

Surgical removal of the eye can be avoided in children with orbital ERMS, which can be treated successfully using combined chemo-radiotherapy. Survival rates of >90% are to be expected after such management [1,5,16]. The late effects of such treatments can, however, be severe, especially in infants. Past radiation complications include pronounced growth disturbances and an increased risk of second cancer [7–11]. These difficulties could be largely avoided by the use of chemotherapy alone, although other early, intermediate, and delayed chemotoxicities could supervene depending on the drugs employed.

Taking these several considerations into account, we chose to use only chemotherapy in treating two infants who were 2 months and 13 months of age at diagnosis. The regimens used, which contained several drugs, produced rapid improvement and total ablation of the malignant cells. The children remain disease-free for periods of

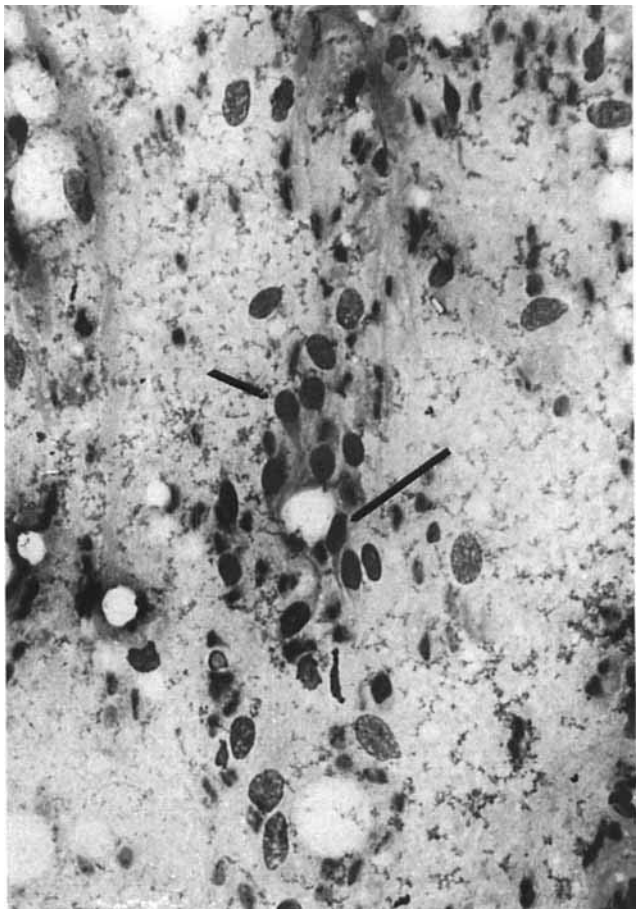

Fig. 4. Case 2. Cytology (needle aspirate). Embryonal rhabdomyosarcoma. Small cells with darkly staining nuclei are visible in the center of the field, some (darts) having the typical "tadpole" configuration.

9 and 5 years, respectively, with no secondary effects attributable to the chemotherapy used. Cosmesis is excellent, and vision is normal in both children. The globe on the affected side in both patients is minimally smaller than its counterpart, and only the strabismus in patient ACM remains.

We wish to point out that the T6 and T6-M protocols incorporate drugs and doses no longer advocated for the treatment of children with ERMS. The total dose of doxorubicin amounts to 480 mg/m^2 after full treatment with the T6 and T6-M regimens, for example. Other chemotherapy combinations known to be effective would be preferable today [12–14].

Nonetheless, we know of no other cases managed successfully in this way, and report this encouraging result as an alternative to be considered when treating infants with orbital ERMS. We would caution extension of chemotherapy alone as a method to be employed in older children or those with larger tumors, where it may not be applicable. In babies, ocular tumors make themselves known when still small because they soon distort and displace the normal structures. It may be that tumors grow to larger size in the deeper, wider orbits of older children before becoming manifest. Given the mixed results of this approach to ERMS in this and other sites [12–14], chemotherapy alone should perhaps only be tried in patients with tumors not greater than 2 cm in diameter until more experience with this method is small tumors is accumulated.

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REFERENCES

1. Álvarez Silván AM, Pineda Cuevas G, Martínez Caro A, Conde García J, Maillo Arcega MA, Martínez Velázquez F, Moreno Rebollo JL: Estado actual del tratamiento del rhabdomiosarcoma en la infancia. Oncología X-51:74–77, 1987.
2. Álvarez Silván AM, Pineda Cuevas G, Martínez Caro A, García Valles MC, Conde García J, Maillo Arcega MA, Martínez Velázquez F, Castelli G: Evaulation of preoperative chemotherapy and radiotherapy of rhabdomyosarcoma in children. Int Pediatr 2:24–26, 1987.
3. García Vallés MC, Álvarez Silván AM, Pineda Cuevas G, Martínez Caro A, Maillo Arcega MA, González del Castillo J: Tratamiento del rhabdomyosarcoma de vejiga sin cirugía radical. An Esp Pediatr 19:501–506, 1983.
4. Hays DM, Lawrence W Jr, Wharam M, Newton W Jr, Ruymann FB, Beltangady M, Maurer HM: Primary re-excision for patients with microscopic residual tumor following initial excision of sarcomas of trunk and extremity sites. J Pediatr Surg 24:5–10, 1989.
5. Maurer HM, Beltanpady M, Gehan EA, Crist W, Hammond D, Hays DM, Heyn R, Lawrence W, Newton W, Ortega J, Ragab AH, Raney RB, Ruymann FB, Soule E, Tefft M, Webber B, Wharam M, Vietti TJ: The Intergroup Rhabdomyosarcoma Study-I: a final report. Cancer 61:209–220, 1988.
6. Tefft M, Wharam M, Gehan E: Local and regional control of rhabdomyosarcoma by radiation in IRS-II. Int J Rad Oncol Biol Phys (Suppl 1) 15:159, 1988.
7. Fromm M, Littman P, Raney B, Nelson L, Handler S, Diamond G, Stanley C: Late effects after treatment of twenty children with soft tissue sarcomas of the head and neck. Cancer 57:2070–2076, 1986.
8. Heyn R, Ragab A, Raney RB Jr, Ruymann F, Tefft M, Lawrence W Jr, Soule E, Maurer HM: Late effects of therapy in orbital rhabdomyosarcoma in children. A report from the Intergroup Rhabdomyosarcoma Study. Cancer 57:1738–1743, 1986.
9. Modan B, Baidatz D, Mart H, Steinitz R, Levin SG: Radiation-induced head and neck tumours. Lancet i:277–279, 1974.
10. Tucker MA, D'Angio GJ, Boice JD, Strong LC, Li FP, Stovall M, Stone BJ, Green D, Lombardi F, Newton W, Hoover RN, Fraumeni JF Jr: Bone sarcoma linked to radiotherapy and chemotherapy in children. N Engl J Med 317:588–593, 1987.
11. Miké V, Meadows AT, D'Angio GJ: Incidence of second malignant neoplasms in children: results of an international study. Lancet ii:1326–1331, 1982.
12. Raney RB, Gehan EA, Hays DM, Tefft M, Newton WA Jr, Maurer HM: Primary chemotherapy with or without radiation

therapy and/or surgery for children with localized sarcoma of the bladder, prostate, vagina, uterus and cervex. A comparison of the results in IRS-I and II. Cancer 66:2077–2081, 1990.
13. Coene IJ, Schouwenberg PF, Voûte PA, Marion J, Burgers V, Hilgers FJ: Rhabdomyosarcoma of the head and neck in children. Clin Otolaryngol 17:291–296, 1992.
14. Rousseau P, Flamant F, Quintana E, Voûte PA, Gentet JC: Primary chemotherapy in rhabdomyosarcomas and other malignant mesenchymal tumors of the orbit: results of the International Society of Pediatric Oncology MMT 84 study. J Clin Oncol 12:516–521, 1994.
15. Ghavimi F, Exelby PR, Jereb B, Lieberman PH, Scott BF, Kosloff C: The multi-disciplinary treatment of advanced stages of embryonal rhabdomyosarcoma in children. Natl Cancer Inst Monogr 56:103–109, 1981.
16. Kingston JE, McElwain TJ, Malpas JS: Childhood rhabdomyosarcoma experience of the Children's Solid Tumour Group. Br J Cancer 48:195–207, 1983.